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 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Apr 08   "Ask CAS" for self-help around the clock
 NEWS  3  Apr 09   BEILSTEIN: Reload and Implementation of a New Subject Area
 NEWS  4  Apr 09   ZDB will be removed from STN
 NEWS  5  Apr 19   US Patent Applications available in IFICDB, IFIPAT, and
IFIUDB
 NEWS  6  Apr 22   Records from IP.com available in CAPLUS, HCAPLUS, and
ZCAPLUS
 NEWS  7  Apr 22   BIOSIS Gene Names now available in TOXCENTER
 NEWS  8  Apr 22   Federal Research in Progress (FEDRIP) now available
 NEWS  9  Jun 03   New e-mail delivery for search results now available
 NEWS 10  Jun 10   MEDLINE Reload
 NEWS 11  Jun 10   PCTFULL has been reloaded
 NEWS 12  Jul 02   FOREGE no longer contains STANDARDS file segment
 NEWS 13  Jul 22   USAN to be reloaded July 28, 2002;
                   saved answer sets no longer valid
 NEWS 14  Jul 29   Enhanced polymer searching in REGISTRY
 NEWS 15  Jul 30   NETFIRST to be removed from STN
 NEWS 16  Aug 08   CANCERLIT reload
 NEWS 17  Aug 08   PHARMAMarketLetter(PHARMAML) - new on STN
 NEWS 18  Aug 08   NTIS has been reloaded and enhanced
 NEWS 19  Aug 19   Aquatic Toxicity Information Retrieval (AQUIRE)
                   now available on STN
 NEWS 20  Aug 19   IFIPAT, IFICDB, and IFIUDB have been reloaded
 NEWS 21  Aug 19   The MEDLINE file segment of TOXCENTER has been reloaded
 NEWS 22  Aug 26   Sequence searching in REGISTRY enhanced
 NEWS 23  Sep 03   JAPIO has been reloaded and enhanced
 NEWS 24  Sep 16   Experimental properties added to the REGISTRY file
 NEWS 25  Sep 16   CA Section Thesaurus available in CAPLUS and CA
 NEWS 26  Oct 01   CASREACT Enriched with Reactions from 1907 to 1985
 NEWS 27  Oct 21   EVENTLINE has been reloaded
 NEWS 28  Oct 24   BEILSTEIN adds new search fields
 NEWS 29  Oct 24   Nutraceuticals International (NUTRACEUT) now available on
STN
 NEWS 30  Oct 25   MEDLINE SDI run of October 8, 2002
 NEWS 31  Nov 18   DKILIT has been renamed APOLLIT
 NEWS 32  Nov 25   More calculated properties added to REGISTRY
 NEWS 33  Dec 02   TIBKAT will be removed from STN
 NEWS 34  Dec 04   CSA files on STN
 NEWS 35  Dec 17   PCTFULL now covers WP/PCT Applications from 1978 to date
 NEWS 36  Dec 17   TOXCENTER enhanced with additional content
 NEWS 37  Dec 17   Adis Clinical Trials Insight now available on STN
 NEWS 38  Dec 30   ISMEC no longer available
 NEWS 39  Jan 21   NUTRACEUT offering one free connect hour in February 2003
 NEWS 40  Jan 21   PHARMAML offering one free connect hour in February 2003
 NEWS 41  Jan 29   Simultaneous left and right truncation added to COMPENDEX,
                   ENERGY, INSPEC
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NEWS 42   Feb 13  CANCERLIT is no longer being updated
NEWS 43   Feb 24  METADEX enhancements
NEWS 44   Feb 24  PCTGEN now available on STN
NEWS 45   Feb 24  TEMA now available on STN
NEWS 46   Feb 26  NTIS now allows simultaneous left and right truncation
NEWS 47   Feb 26  PCTFULL now contains images
NEWS 48   Mar 04  SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 49   Mar 19  APOLLIT offering free connect time in April 2003
NEWS 50   Mar 20  EVENTLINE will be removed from STN
NEWS 51   Mar 24  PATDPAFULL now available on STN
NEWS 52   Mar 24  Additional information for trade-named substances without
                  structures available in REGISTRY
NEWS 53   Mar 24  Indexing from 1957 to 1966 added to records in CA/CAPLUS

NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
              MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
              AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
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NEWS INTER    General Internet Information
NEWS LOGIN    Welcome Banner and News Items
NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
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FILE COVERS 1907 - 10 Apr 2003  VOL 138 ISS 15
FILE LAST UPDATED: 9 Apr 2003  (20030409/ED)
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This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> cyclosporin (w) A
         12961 CYCLOSPORIN
           350 CYCLOSPORINS
         12994 CYCLOSPORIN
                 (CYCLOSPORIN OR CYCLOSPORINS)
      16988954 A
L1       10808 CYCLOSPORIN (W) A

=> "hepatitis B" and L1
         37676 "HEPATITIS"
       1343870 "B"
         13797 "HEPATITIS B"
                 ("HEPATITIS"(W)"B")
L2          18 "HEPATITIS B" AND L1

=> DIS L2 1- IBIB ABS
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L2   ANSWER 1 OF 18  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:        2002:725172  CAPLUS
DOCUMENT NUMBER:         137:261548
TITLE:                   Adoptive transfer of HBV immunity by kidney
                         transplantation and the effect of postoperative
                         vaccination
AUTHOR(S):               Dahmen, Uta; Gu, Yanli; Dirsch, Olaf; Li, Jun;
                         Polywka, Susanne; Doebel, Lothar; Shen, Kai;
Broelsch,
                         Christoph Erich
CORPORATE SOURCE:        Department of General and Transplantation Surgery,
                         University Hospital Essen, Essen, Germany
SOURCE:                  Antiviral Research (2002), 56(1), 29-37
                         CODEN: ARSRDR; ISSN: 0166-3542
PUBLISHER:               Elsevier Science B.V.
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   Transfer of hepatitis B immunity occurs upon the
     transfer of immunol. active cells from the donor to the recipient by
means
     of an organ graft. This has been repeatedly demonstrated for bone marrow
     and liver transplantation. Evidence is now presented for the transfer of
     anti-hepatitis B surface antibodies (anti-HBs) after
     kidney transplantation in rats. Kidney donors from one syngeneic and two
     allogeneic rat strains were immunized twice with 4 .mu.g of recombinant
     hepatitis B vaccine. In week 6 after the first
     vaccination, kidney grafts were transplanted into Lewis (LEW) rats. Half
     of the recipients underwent daily immunosuppressive treatment with
     cyclosporin A (CsA). All recipients were vaccinated
     either after 10 wk or 1 wk postoperatively. Anti-HBs titer was measured
     weekly. Effective anti-HBs titers (10-227 mIU/mL, lasting for 1-7 wk)
     were detected in 86% (25/29) of recipient rats, whose corresponding
donors
     all had a titer above 15,000 mIU/mL. Immunosuppression enhanced the
     donor-derived immunity in terms of recipient-to-donor titer ratio,
maximal
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titer and titer persistence.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L2 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:721049 CAPLUS
DOCUMENT NUMBER: 138:53452
TITLE: Mitochondrial Alterations Induced by the p13II Protein
of Human T-cell Leukemia Virus Type 1. Critical role of arginine residues
AUTHOR(S): D'Agostino, Donna M.; Ranzato, Laura; Arrigoni, Giorgio; Cavallari, Ilaria; Belleudi, Francesca; Torrisi, Maria Rosaria; Silic-Benussi, Micol; Ferro, Tiziana; Petronilli, Valeria; Marin, Oriano; Chieco-Bianchi, Luigi; Bernardi, Paolo; Ciminale, Vincenzo
CORPORATE SOURCE: Dep. Oncol. and Surg. Sci., Univ. Padova, Padua, 35128, Italy
SOURCE: Journal of Biological Chemistry (2002), 277(37), 34424-34433
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human T-cell leukemia virus type 1 encodes a no. of "accessory" proteins of unclear function; one of these proteins, p13II, is targeted to mitochondria and disrupts mitochondrial morphol. The present study was undertaken to unravel the function of p13II through (i) detn. of its submitochondrial localization and sequences required to alter mitochondrial morphol. and (ii) an assessment of the biophys. and biol. properties of synthetic peptides spanning residues 9-41 (p139-41), which include the amphipathic mitochondrial-targeting sequence of the protein. P139-41 folded into an .alpha. helix in micellar environments. Fractionation and immunogold labeling indicated that full-length p13II accumulates in the inner mitochondrial membrane. P139-41 induced energy-dependent swelling of isolated mitochondria by increasing inner membrane permeability to small cations (Na+, K+) and released Ca2+ from Ca2+-preloaded mitochondria. These effects as well as the ability of full-length p13II to alter mitochondrial morphol. in cells required the presence of four arginines, forming the charged face of the targeting signal. The mitochondrial effects of p139-41 were insensitive to **cyclosporin A**, suggesting that full-length p13II might alter mitochondrial permeability through a permeability transition pore-independent mechanism, thus distinguishing it from the mitochondrial proteins Vpr and X of human immunodeficiency virus type 1 and **hepatitis B** virus, resp.
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L2 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:334594 CAPLUS
DOCUMENT NUMBER: 137:41290
TITLE: Lamivudine treatment for acute exacerbation of **hepatitis B** in patients undergoing

immunosuppressive therapy
AUTHOR(S): Kanai, Naoko; Hasegawa, Kiyoshi; Ogawa, Miho; Naritomi, Takuma; Hayashi, Naoaki
CORPORATE SOURCE: Department of Medicine, Tokyo Women's Medical University, Tokyo, 162-8666, Japan
SOURCE: Hepatology Research (2002), 22(3), 223-230
CODEN: HPRSFM; ISSN: 1386-6346
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Lamivudine was administrated to six patients with acute exacerbation of **hepatitis B** who were undergoing immunosuppressive therapy. All patients had chronic **hepatitis B** and were receiving immunosuppressive therapy for other primary diseases (hematol. malignancies, collagen diseases, renal transplantation) when the hepatitis flared up. Only one patient tested pos. for the **hepatitis B** virus e (HBe) antigen. All patients had normal ALT levels and were anti-HBe-pos. before immunosuppressive therapy. The patients were treated with 150 mg of lamivudine daily. Lamivudine was well tolerated and showed no effect on the primary disease. In all patients, **hepatitis B** virus (HBV) DNA levels decreased in response to lamivudine administration. Four patients recovered from exacerbation, but two patients died from complications. Mol. anal. revealed that, regardless of whether patients had the wild HBV genotype or mutations within the core promoter or precore HBV regions, the effectiveness of lamivudine therapy was the same. These results demonstrated that lamivudine is very effective for treating acute exacerbation of chronic **hepatitis B** that occurs while a patient is undergoing immunosuppressive therapy, regardless of the phenotype of the virus.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:294165 CAPLUS
DOCUMENT NUMBER: 136:304036
TITLE: Inhibition of the Src kinase family pathway as a method of treating HBV infection and hepatocellular carcinoma
INVENTOR(S): Schneider, Robert J.; Klein, Nicola
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 37 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002045191	A1	20020418	US 2001-955006	20010917

PRIORITY APPLN. INFO.: US 2000-232892P P 20000915

AB The present invention relates to therapeutic protocols and pharmaceutical compns. designed to target HBx mediated activation of Src kinase, members

of the Src tyrosine kinase family and components of the Src kinase family signal transduction pathways for the treatment of HBV (**hepatitis B** virus) infection and related disorders and diseases, such as hepatocellular carcinoma (HCC). The invention further relates to pharmaceutical compns. for the treatment of HBV infection targeted to HBx and its essential activities required to sustain HBV replication. The invention is based, in part, on the Applicants' discovery that activation of Src kinase signaling cascades play a fundamental role in mammalian hepadnavirus replication. Applicants have demonstrated that HBx mediates activation of the Src family of kinases and that this activation is a crit. function provided by HBx for mammalian hepadnavirus replication.

L2 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:158385 CAPLUS
DOCUMENT NUMBER: 136:205441
TITLE: Enantiomers of S-adenosyl-L-methionine
INVENTOR(S): Hebert, Rolland F.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 7 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002025926	A1	20020228	US 2001-943243	20010830

PRIORITY APPLN. INFO.: US 2000-229151P P 20000830
AB Enantiomers of S-adenosyl-l-methionine, their stable salts and their uses are described. These compns. possess potent activity in treating various conditions involving hypomethylation and transulfuration reactions and are valuable for use as active constituents in pharmaceutical compns. For example, (S,S)-S-adenosylmethionine was prepd. and stabilized using p-toluene sulfonate. (S,S)-S-adenosylmethionine enteric-coated tablets (400 mg) were administered twice daily for 14 days or until remission of depression symptoms in an open, non-blind study to 10 volunteers (one patient declined to continue the study after beginning). All patients had normal results on pre-study medical examns., including lab. examns. Eight of the nine patients who completed the trial improved over the 14 days, while one patient had no change at all. No side effects were noted or reported by any of the patients nor as measured by lab. or phys. examn. (S, S)-S-adenosylmethionine 400 mg twice daily appeared to be safe and effective in this small, non-blinded study of depression.

L2 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:851786 CAPLUS
DOCUMENT NUMBER: 136:4707
TITLE: Immunostimulatory nucleic acids for inducing a Th2 immune response
INVENTOR(S): McCluskie, Michael J.; Davis, Heather L.
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 50 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001044416	A1	20011122	US 2001-768012	20010122
WO 2001095935	A1	20011220	WO 2001-US2170	20010122

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-177461P P 20000120

AB The invention relates to methods and products for inducing an immune response using immunostimulatory nucleic acids. In particular the immunostimulatory nucleic acids preferentially induce a Th2 immune response. The invention is useful for treating and preventing disorders assocd. with a Th1 immune response or for creating a Th2 environment for treating disorders that are sensitive to Th2 immune responses. These disorders include Th1-mediated disease, autoimmune disease, infection, and cancer.

L2 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:699548 CAPLUS

DOCUMENT NUMBER: 136:2662

TITLE: Nuclear factor of activated T cells (NFAT1-C) represses the enhancer II and pregenomic promoter (EnII/Cp) of **hepatitis B** virus (HBV) through its responsive site GGAGA and nullifies the HBx-driven transcriptional activation

AUTHOR(S): Lee, Joong Hyuk; Rho, Hyune Mo

CORPORATE SOURCE: School of Biological Sciences, Seoul National University, Seoul, 151-742, S. Korea

SOURCE: IUBMB Life (2001), 51(4), 255-261
CODEN: IULIF8; ISSN: 1521-6543

PUBLISHER: Taylor & Francis

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The immunosuppressant **cyclosporin A** (CsA)-sensitive nuclear factor of activated T cells 1 (NFAT1) has been known to be a transcriptional regulator of cytokine and viral genes during the immune response. By analyses of serial deletion, mutation, and heterologous promoter assay, the authors report here that the CsA-sensitive NFAT1-C represses the transcriptional activity of enhancer II and pregenomic promoter (EnII/Cp) of HBV through the NFAT1-C responsive site (GGAGA, nt 1603-1618) and nullifies the HBx-driven transcriptional activation of the EnII/Cp of HBV in a dose-dependent manner. These results suggest that a CsA-sensitive NFAT1-C may control the viral activity in HBV-infected cells by inhibiting the EnII/Cp and nullifying the HBx-driven transcriptional activation.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:300514 CAPLUS
DOCUMENT NUMBER: 134:331617
TITLE: Oil-in-water emulsion compositions for polyfunctional active ingredients
INVENTOR(S): Chen, Feng-jing; Patel, Mahesh V.
PATENT ASSIGNEE(S): Lipocine, Inc., USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001028555	A1	20010426	WO 2000-US28835	20001018
US 2002107265	A1	20020808	US 1999-420159	19991018

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-420159 A 19991018

AB Pharmaceutical oil-in-water emulsions for delivery of polyfunctional active ingredients with improved loading capacity, enhanced stability, and reduced irritation and local toxicity are described. Emulsions include an aq. phase, an oil phase comprising a structured triglyceride, and an emulsifier. The structured triglyceride of the oil phase is substantially free of triglycerides having three medium chain (C6-C12) fatty acid moieties, or a combination of a long chain triglyceride and a polarity-enhancing polarity modifier. The present invention also provides methods of treating an animal with a polyfunctional active ingredient, using dosage forms of the pharmaceutical emulsions. For example, an emulsion was prepd., with **cyclosporin A** as the polyfunctional active ingredient dissolved in an oil phase including a structured triglyceride (Captex 810D) and a long chain triglyceride (safflower oil). The compn. contained (by wt.) **cyclosporin A** 1.0, Captex 810D 5.0, safflower oil 5.0, BHT 0.02, egg phospholipid 2.4, dimyristoylphosphatidyl glycerol 0.2, glycerol 2.25, EDTA 0.01, and water up to 100%, resp.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:209222 CAPLUS
DOCUMENT NUMBER: 135:298361
TITLE: Influence of CsA treatment on adoptive transfer of immunity after allogeneic kidney transplantation in rats
AUTHOR(S): Gu, Y. L.; Dahmen, U.; Doebel, L.; Li, J.; Dirsch, O.;

Polywka, S.; Broelsch, C. E.
CORPORATE SOURCE: Department of General and Transplantation Surgery, University Hospital of Essen, Essen, Germany
SOURCE: Transplantation Proceedings (2001), 33(1-2), 398-400
CODEN: TRPPA8; ISSN: 0041-1345
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The efficacy of adoptive transfer of immunity by allogeneic kidney transplantation and the influence of immunosuppressive treatment on the adoptive immune transfer were studied in rats. All donor animals developed a high titer after vaccination with no statistically considerable difference between the two groups. Kidney recipients under immunosuppressive treatment with cyclosporine developed a much higher anti-**hepatitis B** (HB) titer and a longer persistence of the effective titer at postoperative day 7 than without treatment. This effect was most likely attributed to the continuous secretion of antibodies by plasma cells which was unaffected by the immunosuppression, while prolongation of the titer persistence might be due to the prolonged presence of plasma cells being protected from rejection. Kidney transplantation from a vaccinated donor led to effective antibody prodn. in the recipient and the anti-HB titer lasted for about 6 wk. The primed passenger lymphocytes within the kidney graft were supposed to play a major role in this adoptive immune transfer through kidney transplantation.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:126746 CAPLUS
DOCUMENT NUMBER: 133:87326
TITLE: The relationship between angiogenesis and the immune response in carcinogenesis and the progression of malignant disease
AUTHOR(S): O'Byrne, K. J.; Dalgleish, A. G.; Browning, M. J.; Steward, W. P.; Harris, A. L.
CORPORATE SOURCE: Leicester Royal Infirmary, University Department of Oncology, Leicester, UK
SOURCE: European Journal of Cancer (2000), 36(2), 151-169
CODEN: EJCAEL; ISSN: 0959-8049
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 263 refs. Recent studies have demonstrated that angiogenesis and suppressed cell-mediated immunity (CMI) play a central role in the pathogenesis of malignant disease facilitating tumor growth, invasion and metastasis. In the majority of tumors, the malignant process is preceded by a pathol. condition or exposure to an irritant which itself is assocd. with the induction of angiogenesis and/or suppressed CMI. These include: cigarette smoking, chronic bronchitis and lung cancer; chronic esophagitis and esophageal cancer; chronic viral infections such as human papilloma virus and ano-genital cancers, chronic **hepatitis B** and C and hepatocellular carcinoma, and Epstein-Barr virus (EBV) and lymphomas; chronic inflammatory conditions such as Crohn's disease and ulcerative colitis and colorectal cancer; asbestos exposure and mesothelioma and excessive sunlight exposure/sunburn

and malignant melanoma. Chronic exposure to growth factors (insulin-like growth factor-I in acromegaly), mutations in tumor suppressor genes (TP53 in Li Fraumeni syndrome) and long-term exposure to immunosuppressive agents (**cyclosporin A**) may also give rise to similar environments and are assocd. with the development of a range of solid tumors. The increased blood supply would facilitate the development and proliferation of an abnormal clone or clones of cells arising as the result of: (a) an inherited genetic abnormality; and/or (b) acquired somatic mutations, the latter due to local prodn. and/or enhanced delivery of carcinogens and mutagenic growth factors. With progressive detrimental mutations and growth-induced tumor hypoxia, the transformed cell, to a lesser or greater extent, may amplify the angiogenic process and CMI suppression, thereby facilitating further tumor growth and metastasis. There is accumulating evidence that long-term treatment with cyclo-oxygenase inhibitors (aspirin and indomethacin), cytokines such as interferon-.alpha., anti-estrogens (tamoxifen and raloxifene) and captopril significantly reduces the incidence of solid tumors such as breast and colorectal cancer. These agents are anti-angiogenic and, in the case of aspirin, indomethacin and interferon-.alpha. have proven immunomodulatory effects. Collectively these observations indicate that angiogenesis and suppressed CMI play a central role in the development and progression of malignant disease.

REFERENCE COUNT: 263 THERE ARE 263 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:348763 CAPLUS

DOCUMENT NUMBER: 131:128436

TITLE: The proapoptotic effect of **hepatitis B** virus HBx protein correlates with its transactivation activity in stably transfected cell lines

AUTHOR(S): Bergametti, Francoise; Prigent, Sylvie; Luber, Birgit; Benoit, Annie; Tiollais, Pierre; Sarasin, Alain; Transy, Catherine

CORPORATE SOURCE: Unite de Recombinaison et Expression Genetique (INSERM U163), Institut Pasteur, Paris, Fr.

SOURCE: Oncogene (1999), 18(18), 2860-2871
CODEN: ONCNES; ISSN: 0950-9232

PUBLISHER: Stockton Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The role of **hepatitis B** virus HBx protein in the carcinogenesis assocd. with chronic viral infection remains ill-defined. Indeed, pleiotropic effects have been ascribed to HBx: in addn. to its well-documented ability to indirectly stimulate transcription, the protein has been reported to affect cell growth, signal transduction, DNA repair and apoptosis. In this work, we generated Chang (CCL-13)-derived cell lines constitutively expressing wild type or mutant HBx, as a model of HBx-host cell interaction closer to the chronic infection setting, than the classically used transient expression systems. We document the potentiation by HBx of the apoptotic cell death pathway in the recipient cells. This effect is unlikely to rely on p53 activity since the protein

is functionally inactivated in CCL-13. In addn., antioxidants and **cyclosporin A** failed to reduce the apoptotic response back to the normal level, suggesting that prodn. of reactive oxygen species and calcineurin activation are not directly involved in the proapoptotic effect of HBx. In contrast, our data show that transactivation and stimulation of apoptosis are tightly linked HBx activities. Finally, expression of transactivation-active protein did not result in detectable change in the pattern of MAP kinases phosphorylation nor did it affect the ability of the host cell to repair in vitro irradiated plasmid DNA.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:29452 CAPLUS
DOCUMENT NUMBER: 130:195699
TITLE: The **hepatitis B** virus X protein activates nuclear factor of activated T cells (NF-AT) by a **cyclosporin A**-sensitive pathway
AUTHOR(S): Lara-Pezzi, Enrique; Armesilla, Angel Luis; Majano, Pedro L.; Redondo, Juan Miguel; Lopez-Cabrera, Manuel
CORPORATE SOURCE: Unidades Biologia Molecular, Universidad Autonoma de Madrid, Madrid, 28006, Spain
SOURCE: EMBO Journal (1998), 17(23), 7066-7077
CODEN: EMJODG; ISSN: 0261-4189
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The X gene product of the human **hepatitis B** virus (HBx) is a transcriptional activator of various viral and cellular genes. We recently have detd. that the prodn. of tumor necrosis factor-.alpha. (TNF-.alpha.) by HBV-infected hepatocytes is transcriptionally up-regulated by HBx, involving nuclear factor of activated T cells (NF-AT)-dependent activation of the TNF-.alpha. gene promoter. Here we show that HBx activates NF-AT by a **cyclosporin A**-sensitive mechanism involving dephosphorylation and nuclear translocation of the transcription factor. Luciferase gene expression assays demonstrated that HBx transactivates transcription through NF-AT-binding sites and activates a Gal4-NF-AT chimeric protein. DNA-protein interaction assays revealed that HBx induces the formation of NF-AT-contg. DNA-binding complexes. Immunofluorescence anal. demonstrated that HBx induces the nuclear translocation of NF-AT, which can be blocked by the immunosuppressive drug **cyclosporin A**. Furthermore, immunoblot anal. showed that the HBx-induced activation and translocation of NF-AT are assocd. with its dephosphorylation. Thus, HBx may play a relevant role in the intrahepatic inflammatory processes by inducing locally the expression of cytokines that are regulated by NF-AT.

REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:484946 CAPLUS

DOCUMENT NUMBER: 129:121659
TITLE: A method of modulating an immune response in an infected mammal by transmucosal administration of modulating agent
INVENTOR(S): Michaels, Frank; Block, Timothy
PATENT ASSIGNEE(S): Thomas Jefferson University, USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9829121	A1	19980709	WO 1998-US4116	19980102
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 979080	A1	20000216	EP 1998-911458	19980102
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001507360	T2	20010605	JP 1998-530372	19980102
US 6355248	B1	20020312	US 1999-334819	19990617

PRIORITY APPLN. INFO.: US 1997-34596P P 19970102
WO 1998-US4116 W 19980102

AB Methods and compns. for modulating an immune response in mammals infected with a bacterium, a virus, or a parasite are provided. The methods and compns. are useful in mammals experiencing acute or chronic infections. The methods and compns. may be used in conjunction with known treatments for infection. The method entails the transmucosal administration of a compn. comprising and epitope. The epitope of the mol. administered may be an epitope located on an antigen of the infectious agent or and epitope located on a tissue of the mammal. Typically, the tissue-derived epitope becomes reactive with the immune system and produces adverse or undesirable effects after the mammal is infected.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:338304 CAPLUS
DOCUMENT NUMBER: 125:1375
TITLE: Combination preparation containing **cyclosporin A** or FK 506 or rapamycin and a xanthine derivative
INVENTOR(S): Schoenharting, Martin; Gebert, Ulrich; Waer, Mark
PATENT ASSIGNEE(S): Hoechst A.-G., Germany; Katholieke Universiteit Leuven
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9605854	A2	19960229	WO 1995-EP3126	19950807

WO 9605854		A3	19960411			
W: AU, CA, CN, CZ, FI, HU, JP, KR, MX, NO, PL, RU, SI, UA, US						
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE						
DE 4430127		A1	19960314	DE 1994-4430127		19940825
CA 2199949		AA	19960229	CA 1995-2199949		19950807
AU 9533428		A1	19960314	AU 1995-33428		19950807
AU 714129		B2	19991216			
EP 797448		A2	19971001	EP 1995-929805		19950807
EP 797448		B1	20030226			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE						
CN 1162919		A	19971022	CN 1995-195562		19950807
CN 1096859		B	20021225			
AT 233095		E	20030315	AT 1995-929805		19950807
US 6046328		A	20000404	US 1997-817218		19970403
US 6432968		B1	20020813	US 1999-437829		19991110
PRIORITY APPLN. INFO.:				DE 1994-4430127	A	19940825
				WO 1995-EP3126	W	19950807
				US 1997-817218	A1	19970403

OTHER SOURCE(S): MARPAT 125:1375

AB Combination prepns. which contain **cyclosporin A**, FK 506, or rapamycin with a xanthine deriv. are suitable for use in organ transplantation, cancer, viral diseases or in autoimmune disorders such as systemic lupus erythematosus, rheumatoid arthritis, psoriasis, pemphigus, atopic dermatitis, myositis, multiple sclerosis, nephrotic syndrome (in particular glomerulonephritis), ulcerative colitis or juvenile diabetes. A superadditive action on lymphocyte proliferation in the mixed human lymphocyte reaction assay was demonstrated with 1-(5-hydroxyhexyl)-3-methyl-7-propylxanthine in combination with **cyclosporin A**, FK 506, or rapamycin.

L2 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1995:872869 CAPLUS
DOCUMENT NUMBER: 123:337203
TITLE: In vitro activation of woodchuck lymphocytes measured by radiopurine incorporation and interleukin-2 production: Implications for modeling immunity and therapy in **hepatitis B** virus infection
AUTHOR(S): Cote, Paul J.; Gerin, John L.
CORPORATE SOURCE: Medical Center, Georgetown University, Rockville, MD, 20852, USA
SOURCE: Hepatology (Philadelphia) (1995), 22(3), 687-99
CODEN: HPTLD9; ISSN: 0270-9139
PUBLISHER: Saunders
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cellular immune responses to **hepatitis B** virus (HBV) play an important role in the resoln. of acute infection. They also influence the course of chronic infection and disease but are inadequate to completely clear the infection. Woodchuck hepatitis virus (WHV) infection of the woodchuck can provide a model to study these processes. Lymphocyte responses of woodchucks were assessed by in vitro proliferation and/or interleukin (IL)-2 assays using mitogen (ConA), cytokine (IL-2), superantigen (Staphylococcus aureus enterotoxin B [SEB]), MHC alloantigen (mixed lymphocyte reaction [MLR]), and viral antigens (woodchuck hepatitis virus core antigen [WHcAg] and woodchuck hepatitis virus surface antigen [WHsAg]). ConA-stimulated woodchuck lymphocytes underwent cell division

based on cell counting expts. and produced IL-2 as detected using an IL-2-dependent murine cell line but failed to incorporate sufficient tritiated thymidine; however, they did incorporate sufficient tritiated adenosine and deoxyadenosine to permit development of a meaningful proliferation assay. The IL-2 assay was sensitive and specific for detection of woodchuck IL-2 induced by mitogen, superantigen, and MLR. **Cyclosporin A** and FK506 specifically inhibited ConA- and SEB-induced IL-2 prodn. by woodchuck lymphocytes. Pos. two-way MLRs were detected by IL-2 prodn. and proliferation assay between woodchucks from different geog. regions, thus indicating divergence among MHC mols.; however, occasional neg. MLR reactions among indigenous pairs of woodchucks indicated that some woodchucks were mutually immunocompatible to some degree. The radioadenosine proliferation assay was sensitive for detecting peripheral blood lymphocyte responses to WHcAg and WHsAg in adult woodchucks with recently resolved acute infections. The above systems should facilitate the design of adoptive therapy and liver transplantation expts. in the woodchuck, and also enable modeling of immune responses that promote and maintain chronic hepadnavirus infection.

L2 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:710042 CAPLUS
DOCUMENT NUMBER: 123:132330
TITLE: Effect of immunosuppressive and antiviral agents on **hepatitis B** virus replication in vitro
AUTHOR(S): McMillan, Janine S.; Shaw, Tim; Angus, Peter W.; Locarnini, Stephen A.
CORPORATE SOURCE: Victorian Infectious Diseases Reference Laboratory, Fairfield Hospital, Fairfield, 3078, Australia
SOURCE: Hepatology (Philadelphia) (1995), 22(1), 36-43
CODEN: HPTLD9; ISSN: 0270-9139
PUBLISHER: Saunders
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Hepatitis B** virus (HBV) DNA-transfected hepatoma cells were incubated with the immunosuppressive agents prednisolone, azathioprine, and **cyclosporin A** (CsA) and the antiviral agents ganciclovir and foscarnet to investigate the effects of these compds. on HBV replication. Prednisolone and azathioprine increased intracellular viral DNA and RNA levels approx. twofold and fourfold, resp. Treatment with CsA did not alter the levels of viral RNA or DNA. A combination of all three immunosuppressive agents increased the level of intracellular viral DNA eightfold, indicating an additive effect. Incubation of the cells in the presence of foscarnet decreased levels of both single-stranded and relaxed circular viral DNA, and in the presence of ganciclovir decreased the levels of relaxed circular viral DNA, predictable effects from their known mechanism of action. The stimulatory effect on viral replication induced by the combination of immunosuppressive agents was substantially inhibited by ganciclovir-foscarnet treatment. These observations could have implications for the management of recurrent HBV infection after liver transplantation.

L2 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:674129 CAPLUS
DOCUMENT NUMBER: 123:47894

TITLE: FK506 and other compounds for inhibition of hepatitis D virus and other viruses
INVENTOR(S): Glenn, Jeffrey S.
PATENT ASSIGNEE(S): Regents of the University of California, USA
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9511992	A1	19950504	WO 1994-US10862	19940926
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9478433	A1	19950522	AU 1994-78433	19940926
US 5605828	A	19970225	US 1995-442322	19950516
US 5707867	A	19980113	US 1995-565085	19951130

PRIORITY APPLN. INFO.: US 1993-144759 19931027
WO 1994-US10862 19940926

AB The macrolide FK506, produced by Fujisawa Pharmaceuticals, is effective in inhibiting the replication of hepatitis D virus. It is believed that replication is inhibited either by virtue of the ability of FK506 to inhibit proline isomerase or otherwise to interfere with the function of a C-terminal proline in a replication factor or by virtue of its interference with RNA replication directly. Results are presented which show that nM concns. of FK506 achieve about 50% inhibition of hepatitis D virus replication. Other claimed proline isomerase inhibitors include rapamycin, **cyclosporin A**, and 506BD.

L2 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:441569 CAPLUS
DOCUMENT NUMBER: 115:41569
TITLE: **Cyclosporin A** modulates the course of woodchuck hepatitis virus infection and induces chronicity
AUTHOR(S): Cote, Paul J.; Korba, Brent E.; Steinberg, Howard; Ramirez-Mejia, Carlos; Baldwin, Betty; Hornbuckle, William E.; Tennant, Bud C.; Gerin, John L.
CORPORATE SOURCE: Med. Cent., Georgetown Univ., Rockville, MD, 20852, USA
SOURCE: Journal of Immunology (1991), 146(9), 3138-44
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Immunosuppression in known to influence the state of chronic **hepatitis B** virus infection, and is thought to increase the risk of developing chronic infection in newly exposed individuals. **Cyclosporin A** (CsA), an immunosuppressive agent that inhibits Th cell function, was administered to woodchucks chronically infected with woodchuck hepatitis virus (WHV), and resulted in a decreased

severity of chronic hepatitis and an increased viremia during the treatment. Adult woodchucks inoculated with WHV and given CsA for 14 wk had increased viremias, decreased acute phase liver injury, and developed chronic infections at a higher rate compared with immunocompetent woodchucks given virus alone (chronicity in seven of seven WHV + CsA + vs. zero of nine WHV + CsA-; $p < 0.001$). These results in a relevant animal model of **hepatitis B** virus infection indicate (1) that liver injury in acute hepadnavirus infections is immune-mediated and not a direct cytopathic effect of virus replication, (2) that Th cells function in the inflammatory response and in the immunol. control of hepadnavirus infection, and (3) that suppression of Th cell function in acute hepadnavirus infection decreases liver injury but alters the outcome of infection in favor of chronicity. These results also suggest continued challenges in the application of CsA in liver transplantation for **hepatitis B** virus-induced diseases.

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


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 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Apr 08   "Ask CAS" for self-help around the clock
 NEWS  3  Apr 09   BEILSTEIN: Reload and Implementation of a New Subject Area
 NEWS  4  Apr 09   ZDB will be removed from STN
 NEWS  5  Apr 19   US Patent Applications available in IFICDB, IFIPAT, and
IFIUDB
 NEWS  6  Apr 22   Records from IP.com available in CAPLUS, HCAPLUS, and
ZCAPLUS
 NEWS  7  Apr 22   BIOSIS Gene Names now available in TOXCENTER
 NEWS  8  Apr 22   Federal Research in Progress (FEDRIP) now available
 NEWS  9  Jun 03   New e-mail delivery for search results now available
 NEWS 10  Jun 10   MEDLINE Reload
 NEWS 11  Jun 10   PCTFULL has been reloaded
 NEWS 12  Jul 02   FOREGE no longer contains STANDARDS file segment
 NEWS 13  Jul 22   USAN to be reloaded July 28, 2002;
                   saved answer sets no longer valid
 NEWS 14  Jul 29   Enhanced polymer searching in REGISTRY
 NEWS 15  Jul 30   NETFIRST to be removed from STN
 NEWS 16  Aug 08   CANCERLIT reload
 NEWS 17  Aug 08   PHARMAMarketLetter(PHARMAML) - new on STN
 NEWS 18  Aug 08   NTIS has been reloaded and enhanced
 NEWS 19  Aug 19   Aquatic Toxicity Information Retrieval (AQUIRE)
                   now available on STN
 NEWS 20  Aug 19   IFIPAT, IFICDB, and IFIUDB have been reloaded
 NEWS 21  Aug 19   The MEDLINE file segment of TOXCENTER has been reloaded
 NEWS 22  Aug 26   Sequence searching in REGISTRY enhanced
 NEWS 23  Sep 03   JAPIO has been reloaded and enhanced
 NEWS 24  Sep 16   Experimental properties added to the REGISTRY file
 NEWS 25  Sep 16   CA Section Thesaurus available in CAPLUS and CA
 NEWS 26  Oct 01   CASREACT Enriched with Reactions from 1907 to 1985
 NEWS 27  Oct 21   EVENTLINE has been reloaded
 NEWS 28  Oct 24   BEILSTEIN adds new search fields
 NEWS 29  Oct 24   Nutraceuticals International (NUTRACEUT) now available on
STN
 NEWS 30  Oct 25   MEDLINE SDI run of October 8, 2002
 NEWS 31  Nov 18   DKILIT has been renamed APOLLIT
 NEWS 32  Nov 25   More calculated properties added to REGISTRY
 NEWS 33  Dec 02   TIBKAT will be removed from STN
 NEWS 34  Dec 04   CSA files on STN
 NEWS 35  Dec 17   PCTFULL now covers WP/PCT Applications from 1978 to date
 NEWS 36  Dec 17   TOXCENTER enhanced with additional content
 NEWS 37  Dec 17   Adis Clinical Trials Insight now available on STN
 NEWS 38  Dec 30   ISMEC no longer available
 NEWS 39  Jan 21   NUTRACEUT offering one free connect hour in February 2003
 NEWS 40  Jan 21   PHARMAML offering one free connect hour in February 2003
 NEWS 41  Jan 29   Simultaneous left and right truncation added to COMPENDEX,
                   ENERGY, INSPEC
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 NEWS 42   Feb 13  CANCERLIT is no longer being updated
 NEWS 43   Feb 24  METADEX enhancements
 NEWS 44   Feb 24  PCTGEN now available on STN
 NEWS 45   Feb 24  TEMA now available on STN
 NEWS 46   Feb 26  NTIS now allows simultaneous left and right truncation
 NEWS 47   Feb 26  PCTFULL now contains images
 NEWS 48   Mar 04  SDI PACKAGE for monthly delivery of multifile SDI results
 NEWS 49   Mar 19  APOLLIT offering free connect time in April 2003
 NEWS 50   Mar 20  EVENTLINE will be removed from STN
 NEWS 51   Mar 24  PATDPAFULL now available on STN
 NEWS 52   Mar 24  Additional information for trade-named substances without
                   structures available in REGISTRY
 NEWS 53   Mar 24  Indexing from 1957 to 1966 added to records in CA/CAPLUS

 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
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                                                       ENTRY    SESSION
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FILE COVERS 1907 - 10 Apr 2003 VOL 138 ISS 15
FILE LAST UPDATED: 9 Apr 2003 (20030409/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> "cyclosporin A" (l) "hepatitis B"
         12961 "CYCLOSPORIN"
           350 "CYCLOSPORINS"
         12994 "CYCLOSPORIN"
                 ("CYCLOSPORIN" OR "CYCLOSPORINS")
      16988954 "A"
         10808 "CYCLOSPORIN A"
                 ("CYCLOSPORIN"(W)"A")
         37676 "HEPATITIS"
       1343870 "B"
         13797 "HEPATITIS B"
                 ("HEPATITIS"(W)"B")
L1          11 "CYCLOSPORIN A" (L) "HEPATITIS B"

=> DIS L1 1- IBIB ABS
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L1   ANSWER 1 OF 11  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:        2002:725172  CAPLUS
DOCUMENT NUMBER:         137:261548
TITLE:                   Adoptive transfer of HBV immunity by kidney
                         transplantation and the effect of postoperative
                         vaccination
AUTHOR(S):               Dahmen, Uta; Gu, Yanli; Dirsch, Olaf; Li, Jun;
                         Polywka, Susanne; Doebel, Lothar; Shen, Kai;
Broelsch,
                         Christoph Erich
CORPORATE SOURCE:        Department of General and Transplantation Surgery,
                         University Hospital Essen, Essen, Germany
SOURCE:                  Antiviral Research (2002), 56(1), 29-37
                         CODEN: ARSRDR; ISSN: 0166-3542
PUBLISHER:               Elsevier Science B.V.
DOCUMENT TYPE:           Journal
LANGUAGE:                English
```

AB Transfer of **hepatitis B** immunity occurs upon the transfer of immunol. active cells from the donor to the recipient by means of an organ graft. This has been repeatedly demonstrated for bone marrow and liver transplantation. Evidence is now presented for the transfer of anti-**hepatitis B** surface antibodies (anti-HBs) after kidney transplantation in rats. Kidney donors from one syngeneic and two allogeneic rat strains were immunized twice with 4 .mu.g of recombinant **hepatitis B** vaccine. In week 6 after the first vaccination, kidney grafts were transplanted into Lewis (LEW) rats. Half of the recipients underwent daily immunosuppressive treatment with **cyclosporin A** (CsA). All recipients were vaccinated either after 10 wk or 1 wk postoperatively. Anti-HBs titer was measured

weekly. Effective anti-HBs titers (10-227 mIU/mL, lasting for 1-7 wk) were detected in 86% (25/29) of recipient rats, whose corresponding donors all had a titer above 15,000 mIU/mL. Immunosuppression enhanced the donor-derived immunity in terms of recipient-to-donor titer ratio, maximal titer and titer persistence.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:721049 CAPLUS

DOCUMENT NUMBER: 138:53452

TITLE: Mitochondrial Alterations Induced by the p13II Protein of Human T-cell Leukemia Virus Type 1. Critical role of arginine residues

AUTHOR(S): D'Agostino, Donna M.; Ranzato, Laura; Arrigoni, Giorgio; Cavallari, Ilaria; Belleudi, Francesca; Torrisi, Maria Rosaria; Silic-Benussi, Micol; Ferro, Tiziana; Petronilli, Valeria; Marin, Oriano; Chieco-Bianchi, Luigi; Bernardi, Paolo; Ciminale, Vincenzo

CORPORATE SOURCE: Dep. Oncol. and Surg. Sci., Univ. Padova, Padua, 35128, Italy

SOURCE: Journal of Biological Chemistry (2002), 277(37), 34424-34433
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Human T-cell leukemia virus type 1 encodes a no. of "accessory" proteins of unclear function; one of these proteins, p13II, is targeted to mitochondria and disrupts mitochondrial morphol. The present study was undertaken to unravel the function of p13II through (i) detn. of its submitochondrial localization and sequences required to alter mitochondrial morphol. and (ii) an assessment of the biophys. and biol. properties of synthetic peptides spanning residues 9-41 (p139-41), which include the amphipathic mitochondrial-targeting sequence of the protein. P139-41 folded into an .alpha. helix in micellar environments. Fractionation and immunogold labeling indicated that full-length p13II accumulates in the inner mitochondrial membrane. P139-41 induced energy-dependent swelling of isolated mitochondria by increasing inner membrane permeability to small cations (Na+, K+) and released Ca2+ from Ca2+-preloaded mitochondria. These effects as well as the ability of full-length p13II to alter mitochondrial morphol. in cells required the presence of four arginines, forming the charged face of the targeting signal. The mitochondrial effects of p139-41 were insensitive to **cyclosporin A**, suggesting that full-length p13II might alter mitochondrial permeability through a permeability transition pore-independent mechanism, thus distinguishing it from the mitochondrial proteins Vpr and X of human immunodeficiency virus type 1 and **hepatitis B** virus, resp.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:334594 CAPLUS
DOCUMENT NUMBER: 137:41290
TITLE: Lamivudine treatment for acute exacerbation of hepatitis B in patients undergoing immunosuppressive therapy
AUTHOR(S): Kanai, Naoko; Hasegawa, Kiyoshi; Ogawa, Miho; Naritomi, Takuma; Hayashi, Naoaki
CORPORATE SOURCE: Department of Medicine, Tokyo Women's Medical University, Tokyo, 162-8666, Japan
SOURCE: Hepatology Research (2002), 22(3), 223-230
CODEN: HPRSFM; ISSN: 1386-6346
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Lamivudine was administrated to six patients with acute exacerbation of hepatitis B who were undergoing immunosuppressive therapy. All patients had chronic hepatitis B and were receiving immunosuppressive therapy for other primary diseases (hematol. malignancies, collagen diseases, renal transplantation) when the hepatitis flared up. Only one patient tested pos. for the hepatitis B virus e (HBe) antigen. All patients had normal ALT levels and were anti-HBe-pos. before immunosuppressive therapy. The patients were treated with 150 mg of lamivudine daily. Lamivudine was well tolerated and showed no effect on the primary disease. In all patients, hepatitis B virus (HBV) DNA levels decreased in response to lamivudine administration. Four patients recovered from exacerbation, but two patients died from complications. Mol. anal. revealed that, regardless of whether patients had the wild HBV genotype or mutations within the core promoter or precore HBV regions, the effectiveness of lamivudine therapy was the same. These results demonstrated that lamivudine is very effective for treating acute exacerbation of chronic hepatitis B that occurs while a patient is undergoing immunosuppressive therapy, regardless of the phenotype of the virus.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:294165 CAPLUS
DOCUMENT NUMBER: 136:304036
TITLE: Inhibition of the Src kinase family pathway as a method of treating HBV infection and hepatocellular carcinoma
INVENTOR(S): Schneider, Robert J.; Klein, Nicola
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 37 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002045191	A1	20020418	US 2001-955006	20010917

PRIORITY APPLN. INFO.: US 2000-232892P P 20000915
AB The present invention relates to therapeutic protocols and pharmaceutical

compns. designed to target HBx mediated activation of Src kinase, members of the Src tyrosine kinase family and components of the Src kinase family signal transduction pathways for the treatment of HBV (hepatitis B virus) infection and related disorders and diseases, such as hepatocellular carcinoma (HCC). The invention further relates to pharmaceutical compns. for the treatment of HBV infection targeted to HBx and its essential activities required to sustain HBV replication. The invention is based, in part, on the Applicants' discovery that activation of Src kinase signaling cascades play a fundamental role in mammalian hepadnavirus replication. Applicants have demonstrated that HBx mediates activation of the Src family of kinases and that this activation is a crit. function provided by HBx for mammalian hepadnavirus replication.

L1 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:699548 CAPLUS
DOCUMENT NUMBER: 136:2662
TITLE: Nuclear factor of activated T cells (NFAT1-C) represses the enhancer II and pregenomic promoter (EnII/Cp) of hepatitis B virus (HBV) through its responsive site GGAGA and nullifies the HBx-driven transcriptional activation
AUTHOR(S): Lee, Joong Hyuk; Rho, Hyune Mo
CORPORATE SOURCE: School of Biological Sciences, Seoul National University, Seoul, 151-742, S. Korea
SOURCE: IUBMB Life (2001), 51(4), 255-261
CODEN: IULIF8; ISSN: 1521-6543
PUBLISHER: Taylor & Francis
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The immunosuppressant cyclosporin A (CsA)-sensitive nuclear factor of activated T cells 1 (NFAT1) has been known to be a transcriptional regulator of cytokine and viral genes during the immune response. By analyses of serial deletion, mutation, and heterologous promoter assay, the authors report here that the CsA-sensitive NFAT1-C represses the transcriptional activity of enhancer II and pregenomic promoter (EnII/Cp) of HBV through the NFAT1-C responsive site (GGAGA, nt 1603-1618) and nullifies the HBx-driven transcriptional activation of the EnII/Cp of HBV in a dose-dependent manner. These results suggest that a CsA-sensitive NFAT1-C may control the viral activity in HBV-infected cells by inhibiting the EnII/Cp and nullifying the HBx-driven transcriptional activation.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:126746 CAPLUS
DOCUMENT NUMBER: 133:87326
TITLE: The relationship between angiogenesis and the immune response in carcinogenesis and the progression of malignant disease
AUTHOR(S): O'Byrne, K. J.; Dalgleish, A. G.; Browning, M. J.; Steward, W. P.; Harris, A. L.
CORPORATE SOURCE: Leicester Royal Infirmary, University Department of Oncology, Leicester, UK
SOURCE: European Journal of Cancer (2000), 36(2), 151-169
CODEN: EJCAEL; ISSN: 0959-8049
PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 263 refs. Recent studies have demonstrated that angiogenesis and suppressed cell-mediated immunity (CMI) play a central role in the pathogenesis of malignant disease facilitating tumor growth, invasion and metastasis. In the majority of tumors, the malignant process is preceded by a pathol. condition or exposure to an irritant which itself is assocd. with the induction of angiogenesis and/or suppressed CMI. These include: cigarette smoking, chronic bronchitis and lung cancer; chronic esophagitis and esophageal cancer; chronic viral infections such as human papilloma virus and ano-genital cancers, chronic **hepatitis B** and C and hepatocellular carcinoma, and Epstein-Barr virus (EBV) and lymphomas; chronic inflammatory conditions such as Crohn's disease and ulcerative colitis and colorectal cancer; asbestos exposure and mesothelioma and excessive sunlight exposure/sunburn and malignant melanoma. Chronic exposure to growth factors (insulin-like growth factor-I in acromegaly), mutations in tumor suppressor genes (TP53 in Li Fraumeni syndrome) and long-term exposure to immunosuppressive agents (**cyclosporin A**) may also give rise to similar environments and are assocd. with the development of a range of solid tumors. The increased blood supply would facilitate the development and proliferation of an abnormal clone or clones of cells arising as the result of: (a) an inherited genetic abnormality; and/or (b) acquired somatic mutations, the latter due to local prodn. and/or enhanced delivery of carcinogens and mutagenic growth factors. With progressive detrimental mutations and growth-induced tumor hypoxia, the transformed cell, to a lesser or greater extent, may amplify the angiogenic process and CMI suppression, thereby facilitating further tumor growth and metastasis. There is accumulating evidence that long-term treatment with cyclo-oxygenase inhibitors (aspirin and indomethacin), cytokines such as interferon-.alpha., anti-estrogens (tamoxifen and raloxifene) and captopril significantly reduces the incidence of solid tumors such as breast and colorectal cancer. These agents are anti-angiogenic and, in the case of aspirin, indomethacin and interferon-.alpha. have proven immunomodulatory effects. Collectively these observations indicate that angiogenesis and suppressed CMI play a central role in the development and progression of malignant disease.
REFERENCE COUNT: 263 THERE ARE 263 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:348763 CAPLUS
DOCUMENT NUMBER: 131:128436
TITLE: The proapoptotic effect of hepatitis B virus HBx protein correlates with its transactivation activity in stably transfected cell lines
AUTHOR(S): Bergametti, Francoise; Prigent, Sylvie; Luber, Birgit; Benoit, Annie; Tiollais, Pierre; Sarasin, Alain; Transy, Catherine
CORPORATE SOURCE: Unite de Recombinaison et Expression Genetique (INSERM U163), Institut Pasteur, Paris, Fr.

SOURCE: Oncogene (1999), 18(18), 2860-2871
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The role of **hepatitis B** virus HBx protein in the carcinogenesis assocd. with chronic viral infection remains ill-defined. Indeed, pleiotropic effects have been ascribed to HBx: in addn. to its well-documented ability to indirectly stimulate transcription, the protein has been reported to affect cell growth, signal transduction, DNA repair and apoptosis. In this work, we generated Chang (CCL-13)-derived cell lines constitutively expressing wild type or mutant HBx, as a model of HBx-host cell interaction closer to the chronic infection setting, than the classically used transient expression systems. We document the potentiation by HBx of the apoptotic cell death pathway in the recipient cells. This effect is unlikely to rely on p53 activity since the protein is functionally inactivated in CCL-13. In addn., antioxidants and **cyclosporin A** failed to reduce the apoptotic response back to the normal level, suggesting that prodn. of reactive oxygen species and calcineurin activation are not directly involved in the proapoptotic effect of HBx. In contrast, our data show that transactivation and stimulation of apoptosis are tightly linked HBx activities. Finally, expression of transactivation-active protein did not result in detectable change in the pattern of MAP kinases phosphorylation nor did it affect the ability of the host cell to repair in vitro irradiated plasmid DNA.
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:29452 CAPLUS
DOCUMENT NUMBER: 130:195699
TITLE: The **hepatitis B** virus X protein activates nuclear factor of activated T cells (NF-AT) by a **cyclosporin A**-sensitive pathway
AUTHOR(S): Lara-Pezzi, Enrique; Armesilla, Angel Luis; Majano, Pedro L.; Redondo, Juan Miguel; Lopez-Cabrera, Manuel
CORPORATE SOURCE: Unidades Biologia Molecular, Universidad Autonoma de Madrid, Madrid, 28006, Spain
SOURCE: EMBO Journal (1998), 17(23), 7066-7077
CODEN: EMJODG; ISSN: 0261-4189
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The X gene product of the human **hepatitis B** virus (HBx) is a transcriptional activator of various viral and cellular genes. We recently have detd. that the prodn. of tumor necrosis factor-.alpha. (TNF-.alpha.) by HBV-infected hepatocytes is transcriptionally up-regulated by HBx, involving nuclear factor of activated T cells (NF-AT)-dependent activation of the TNF-.alpha. gene promoter. Here we show that HBx activates NF-AT by a **cyclosporin A**-sensitive mechanism involving dephosphorylation and nuclear translocation of the transcription factor. Luciferase gene expression assays demonstrated that HBx transactivates transcription through NF-AT-binding

sites and activates a Gal4-NF-AT chimeric protein. DNA-protein interaction assays revealed that HBx induces the formation of NF-AT-contg. DNA-binding complexes. Immunofluorescence anal. demonstrated that HBx induces the nuclear translocation of NF-AT, which can be blocked by the immunosuppressive drug **cyclosporin A**. Furthermore, immunoblot anal. showed that the HBx-induced activation and translocation of NF-AT are assocd. with its dephosphorylation. Thus, HBx may play a relevant role in the intrahepatic inflammatory processes by inducing locally the expression of cytokines that are regulated by NF-AT.

REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1995:872869 CAPLUS
DOCUMENT NUMBER: 123:337203
TITLE: In vitro activation of woodchuck lymphocytes measured by radiopurine incorporation and interleukin-2 production: Implications for modeling immunity and therapy in hepatitis B virus infection
AUTHOR(S): Cote, Paul J.; Gerin, John L.
CORPORATE SOURCE: Medical Center, Georgetown University, Rockville, MD, 20852, USA
SOURCE: Hepatology (Philadelphia) (1995), 22(3), 687-99
CODEN: HPTLD9; ISSN: 0270-9139
PUBLISHER: Saunders
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cellular immune responses to **hepatitis B** virus (HBV) play an important role in the resoln. of acute infection. They also influence the course of chronic infection and disease but are inadequate to completely clear the infection. Woodchuck hepatitis virus (WHV) infection of the woodchuck can provide a model to study these processes. Lymphocyte responses of woodchucks were assessed by in vitro proliferation and/or interleukin (IL)-2 assays using mitogen (ConA), cytokine (IL-2), superantigen (Staphylococcus aureus enterotoxin B [SEB]), MHC alloantigen (mixed lymphocyte reaction [MLR]), and viral antigens (woodchuck hepatitis virus core antigen [WHcAg] and woodchuck hepatitis virus surface antigen [WHsAg]). ConA-stimulated woodchuck lymphocytes underwent cell division based on cell counting expts. and produced IL-2 as detected using an IL-2-dependent murine cell line but failed to incorporate sufficient tritiated thymidine; however, they did incorporate sufficient tritiated adenosine and deoxyadenosine to permit development of a meaningful proliferation assay. The IL-2 assay was sensitive and specific for detection of woodchuck IL-2 induced by mitogen, superantigen, and MLR. **Cyclosporin A** and FK506 specifically inhibited ConA- and SEB-induced IL-2 prodn. by woodchuck lymphocytes. Pos. two-way MLRs were detected by IL-2 prodn. and proliferation assay between woodchucks from different geog. regions, thus indicating divergence among MHC mols.; however, occasional neg. MLR reactions among indigenous pairs of woodchucks indicated that some woodchucks were mutually immunocompatible to some degree. The radioadenosine proliferation assay was sensitive for detecting peripheral blood lymphocyte responses to WHcAg and WHsAg in adult woodchucks with recently resolved acute infections. The above systems should facilitate the design of adoptive therapy and liver transplantation expts. in the woodchuck, and also enable modeling of

immune responses that promote and maintain chronic hepadnavirus infection.

L1 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:710042 CAPLUS
DOCUMENT NUMBER: 123:132330
TITLE: Effect of immunosuppressive and antiviral agents on hepatitis B virus replication in vitro
AUTHOR(S): McMillan, Janine S.; Shaw, Tim; Angus, Peter W.; Locarnini, Stephen A.
CORPORATE SOURCE: Victorian Infectious Diseases Reference Laboratory, Fairfield Hospital, Fairfield, 3078, Australia
SOURCE: Hepatology (Philadelphia) (1995), 22(1), 36-43
CODEN: HPTLD9; ISSN: 0270-9139
PUBLISHER: Saunders
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Hepatitis B** virus (HBV) DNA-transfected hepatoma cells were incubated with the immunosuppressive agents prednisolone, azathioprine, and **cyclosporin A** (CsA) and the antiviral agents ganciclovir and foscarnet to investigate the effects of these compds. on HBV replication. Prednisolone and azathioprine increased intracellular viral DNA and RNA levels approx. twofold and fourfold, resp. Treatment with CsA did not alter the levels of viral RNA or DNA. A combination of all three immunosuppressive agents increased the level of intracellular viral DNA eightfold, indicating an additive effect. Incubation of the cells in the presence of foscarnet decreased levels of both single-stranded and relaxed circular viral DNA, and in the presence of ganciclovir decreased the levels of relaxed circular viral DNA, predictable effects from their known mechanism of action. The stimulatory effect on viral replication induced by the combination of immunosuppressive agents was substantially inhibited by ganciclovir-foscarnet treatment. These observations could have implications for the management of recurrent HBV infection after liver transplantation.

L1 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:441569 CAPLUS
DOCUMENT NUMBER: 115:41569
TITLE: Cyclosporin A modulates the course of woodchuck hepatitis virus infection and induces chronicity
AUTHOR(S): Cote, Paul J.; Korba, Brent E.; Steinberg, Howard; Ramirez-Mejia, Carlos; Baldwin, Betty; Hornbuckle, William E.; Tennant, Bud C.; Gerin, John L.
CORPORATE SOURCE: Med. Cent., Georgetown Univ., Rockville, MD, 20852, USA
SOURCE: Journal of Immunology (1991), 146(9), 3138-44
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Immunosuppression in known to influence the state of chronic **hepatitis B** virus infection, and is thought to increase the risk of developing chronic infection in newly exposed individuals. **Cyclosporin A** (CsA), an immunosuppressive agent that inhibits Th cell function, was administered to woodchucks chronically infected with woodchuck hepatitis virus (WHV), and resulted in a decreased

severity of chronic hepatitis and an increased viremia during the treatment. Adult woodchucks inoculated with WHV and given CsA for 14 wk had increased viremias, decreased acute phase liver injury, and developed chronic infections at a higher rate compared with immunocompetent woodchucks given virus alone (chronicity in seven of seven WHV + CsA + vs. zero of nine WHV + CsA-; p < 0.001). These results in a relevant animal model of **hepatitis B** virus infection indicate (1) that liver injury in acute hepadnavirus infections is immune-mediated and not a direct cytopathic effect of virus replication, (2) that Th cells function in the inflammatory response and in the immunol. control of hepadnavirus infection, and (3) that suppression of Th cell function in acute hepadnavirus infection decreases liver injury but alters the outcome of infection in favor of chronicity. These results also suggest continued challenges in the application of CsA in liver transplantation for **hepatitis B** virus-induced diseases.

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